

Amendments to the Specification:

Please replace the last paragraph at page 26 with the following amended paragraphs:

hnRNP proteins are highly conserved throughout the vertebrates, as well as having sequence homologies in the invertebrate *Drosophila* (Amrein *et al.*, 1988; Robinow and White, 1988) (Bell *et al.*, 1991; Dreyfuss *et al.*, 1993; Inoue *et al.*, 1990; Kay *et al.*, 1990; Roth *et al.*, 1991; Voelker *et al.*, 1990; Von Besser, 1990), and are the most abundant proteins found in the nucleus (Dreyfuss, 1986, Dreyfuss, 1993). In HeLa cells two-dimensional gel electrophoresis has resolved 20 major groups of proteins. These proteins are designated as the heterogeneous nuclear ribonucleoproteins (hnRNPs) A1 (~34kDa) to hnRNP U (~ 120kDa), and categorized by structural motifs (Cobianchi, 1990; Dreyfuss *et al.*, 1993; Matunis *et al.*, 1992; Pinol-Roma *et al.*, 1988). Furthermore, sequence analysis has determined that hnRNPs have one or more RNA-binding modules referred to as the RNP motif or RNA Recognition Motif (RRM) in addition to at least one other auxiliary domain (Dreyfuss *et al.*, 1993). The RNP motif contains two consensus sequences, RNP1 and RNP2, within a domain of approximately 90 amino acid residues that are located about 30 amino acids from each other (Dreyfuss *et al.*, 1993; Dreyfuss *et al.*, 1988). The RNP 1 module is an octapeptide, Lys/Arg-Gly-Phe/Tyr-Gly/Ala-Phe-Val-X-Phen/Tyr, SEQ ID NO: 7 in the Sequence Listing (Adam *et al.*, 1986; Dreyfuss *et al.*, 1993), while the RNP2 module is a hexapeptide rich in aromatic and aliphatic amino acids and is less well conserved (Dreyfuss *et al.*, 1993; Dreyfuss *et al.*, 1988). Both of these consensus sequences are directly related to RNA binding (Dreyfuss *et al.*, 1993; Merrill *et al.*, 1988).

Please replace the last paragraph at page 32 and the first paragraph at page 33 with the following amended paragraphs:

The ESS of the human *FGFR2* pre-mRNA contains a UAGG sequence in the *kgfr* exon (keratinocyte growth factor receptor-exon 8)(Del Gatto, 1996; Del Gatto and Breathnach, 1995;

Del Gatto-Konczak *et al.*, 1999). This sequence has homology to the high affinity consensus sequence 5'-UAGGGA/U-3' recognized by hnRNP A1 (Del Gatto-Konczak *et al.*, 1999). In *in vitro* studies, Del Gatto-Konczak *et al.* (1999) have demonstrated that hnRNP A1 can modulate splice choices by binding to a 10 mer ESS designated S10 (5'-UAGGGCAGGC-3', SEQ ID NO: 5 in the Sequence Listing) or to a 6 mer ESS designated S6 (5'-UAGGGC-3').

In *in vitro* studies, RNA molecules containing the splicing silencer sequence from the human fibroblast receptor 2 *kgfr* exon (*IIIb*) were capable of directing splice choice selection by the recruitment hnRNP A1 (Del Gatto-Konczak *et al.*, 1999). When the following point mutations were introduced into the S6 ESS UCGGGC or UACGGC a two-fold decrease in hnRNP A1 binding was detected (Del Gatto-Konczak *et al.*, 1999). Furthermore, it was determined that the targeting of hnRNP A1 to the ESS domain was through the glycine-rich motif at the C-terminus of the protein. In the human hnRNP A1 protein, the glycine-rich domains are found between residues 189-320: the RGG motif is specifically located at residues 189-247, followed by another glycine-rich motif from residues 239-320 (Del Gatto-Konczak *et al.*, 1999). Silencing of the *k-sam* (*kgfr*) exon in these *in vitro* studies required the entire glycine-rich motif. By examining the corresponding sequence in the chicken *kgfr* exon (*IIIb* exon 8) of *fgfr2* it has been determined that the sequence corresponding to the human ESS is 5'-UAGGGAGGGC-3', SEQ ID NO: 6 in the Sequence Listing).

Please replace or insert the Sequence Listing with the paper copy of the Sequence Listing provided herewith.